



E212

JACC March 12, 2013

Volume 61, Issue 10

## Acute Coronary Syndromes

### TICAGRELOR-INDUCED BLEEDING IN MICE CAN BE REVERSED BY FVIIA (NOVOSEVEN®) AND FII

Poster Contributions

Poster Sessions, Expo North

Monday, March 11, 2013, 9:45 a.m.-10:30 a.m.

---

Session Title: Acute Coronary Syndromes: Basic V

Abstract Category: 2. Acute Coronary Syndromes: Basic

Presentation Number: 1300-188

---

Authors: Sven Nylander, Susanne Pehrsson, Kenny Hansson, AstraZeneca R&D, Mölndal, Sweden

**Background:** Anti-platelet therapy is given to patients with acute coronary syndrome to reduce the risk for thrombotic events but may increase the risk for bleeding. There are limited treatment options if severe bleeding occurs in patients on anti-platelet therapy including ticagrelor.

**Methods:** Ticagrelor, 1.2 mg/kg followed by 30 µg/kg/min, was administered iv to C57Bl6 mice. Cumulative blood loss and bleeding time were measured after cutting 5 mm from the tip of the tail, 20 min post start of ticagrelor infusion. The tail was placed in a hemoglobin sensitive device measuring light absorbance over time at 525 nm for 35 min. NovoSeven®, 1 mg/kg (study 1), or vehicle was given iv once bleeding had commenced, within 90 sec after tail cut. A second study, designed as for NovoSeven®, was performed with recombinant human FII, 10mg/kg (study 2).

**Results:** Study 1: Ticagrelor resulted in >98% inhibition of ex vivo ADP-induced platelet aggregation and increased median blood loss from 122 to 909 abs\*sec which was reversed to 397 abs\*sec (65% reduction p<0.05) by NovoSeven®. Also ticagrelor-induced prolongation of median bleeding time, from 449 to 2003 sec, was reversed by NovoSeven®, to 884 sec (72% reduction p<0.01). Study 2: Ticagrelor increased median blood loss and bleeding time from 71 to 362 abs\*sec and from 613 to 1847 sec, respectively. FII reduced blood loss and bleeding time to 178 abs\*sec (63% reduction) and 701 sec (93% reduction), respectively, levels not significantly different from untreated controls or ticagrelor-treated mice.

**Conclusions:** In mice dosed to complete P2Y<sub>12</sub> inhibition, potentiating coagulation by administration of NovoSeven®, or FII, within 90 sec after bleeding initiation can partly reverse ticagrelor-induced bleeding. These mice data need to be confirmed in man.